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Achieving responsible medicines use at practice and farm level

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Practice management and decision making

Introduction

Achieving responsible and sustainable medicines use in farm animal practice is a significant and timely challenge that veterinary and human health professionals must tackle together (Department of Health, 2013, O'Neill, 2015). Though responsible antimicrobial (AM) use should be of primary importance, to focus on it alone is too narrow an approach, and risks missing the benefits of achieving a more holistic understanding of medicines use on farm in achieving improved animal health and welfare. For example, non-steroidal anti-inflammatory drug (NSAID) use can provide valuable insight into animal welfare and pain management, while the level of implementation of vaccination protocols can establish whether attitudes are geared towards preventive or reactive approaches.

The starting point must be to understand current patterns of prescribing by veterinary surgeons (VS) (Newman and others 2011, Gibbons and others 2013) and actual use on farms, which may not be the same as the intended use. Though progress has been made, the twin challenges of confronting partial compliance with treatment protocols (Sawant and others 2005) and capturing accurate farm-level data on medicines use remain (Department of Health 2014).

Sawant and others (2005) found that on 93% of 113 dairy farms surveyed in Pennsylvania, antibiotics were administered by farm staff rather than the VS and only 32% of producers sought veterinary advice before administration. In the same study only 24% of producers said that they always completed a course of antibiotic (Sawant and others, 2005). However, this is something that industry is taking seriously. In a more recent UK survey of dairy farmers (Jones and others 2015), 100% of respondents had either reduced or planned to reduce antibiotic use. Seventy percent thought that reducing antibiotic usage was a good thing to do with VS being the most influential source of information. Farmers that received a greater proportion of their income from milk production or were more likely to remain in milk production were more likely to demonstrate a positive intention to reduce antibiotic use (Jones and others 2015). This demonstrates that there is clear recognition amongst dairy farmers that this is an important aspect of herd health management (HHM) and VS are well-placed to drive change in this area.

Although prescription only medicines (POM-V) are often administered to farm animals by farm staff, the line of responsibility for their use is clear: it is the VS who must prescribe, only after performing a clinical assessment of an animal or group of animals and establishing a diagnosis, and ensure that the medicines are used correctly. Clear guidelines have been produced (British Veterinary Association 2009, Royal College of Veterinary Surgeons 2012). This responsibility is currently shared between practitioners working for a diverse range of privately owned and often competing veterinary businesses.

At the coal face, establishing responsible medicines use is an essential part of HHM, practice clinical governance and the practise of evidence-based veterinary medicine (EBVM) (Figure 1).

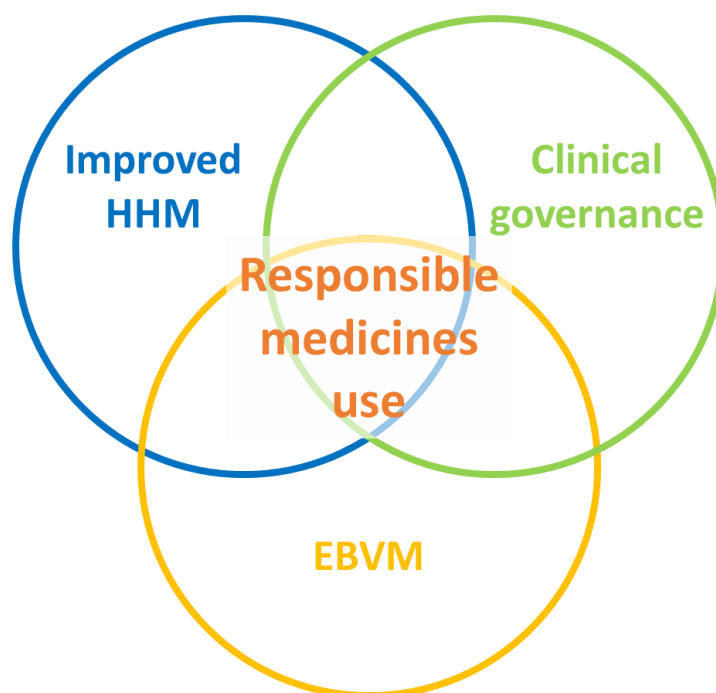


Figure 1. Establishing responsible medicines use

- Improved HHM – Improving farm animal health and welfare by cultivating better farm management practices.** These measures help to reduce disease alongside developing evidence-based and responsible standard treatment protocols, and should mean that fewer treatments are required and when used they are applied appropriately. This is particularly important in farm animal practice because the majority of treatments are AMs and so improved HHM should ultimately reduce AM use and with it the drive towards AMR development. This should be a continuous and adaptive process (Figure 2), built upon an ongoing and collaborative dialogue between the VS and farmer, both of whom can bring their expertise together to improve HHM.

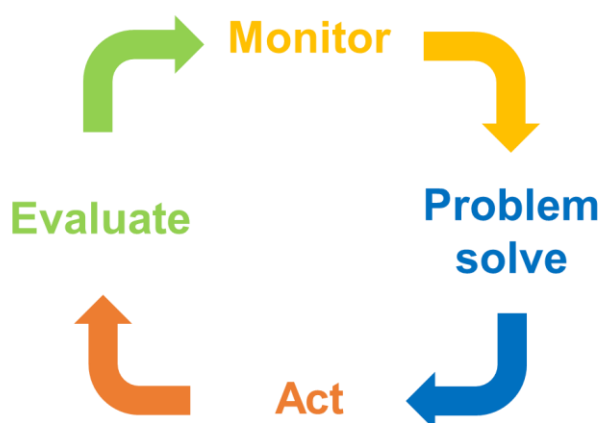


Figure 2. Cycle of HHM and clinical governance

- Practice clinical governance –** Given that AM prescribing constitutes a significant proportion of veterinary treatments, their use and AMR must be considered as part of clinical governance. Monitoring treatment outcomes - both successes and failures - and reviewing protocols accordingly are essential pillars of responsible veterinary practice and part of applying EBVM. The starting point

should be to establish baseline patterns of medicines usage at practice-level alongside simple measures of treatment outcome for common and important conditions. Again this should form part of a continuous cycle of improvement (Figure 2).

- **Evidence-based veterinary medicine (EBVM)** – An evidence-based approach will help to ensure that medicines are only prescribed when they are indicated, and that the most-appropriate treatment is selected.

The World Health Organisation (WHO) has categorised AMs with respect to their importance in terms of human health (WHO, 2012). The two criteria used to group AMs are described in Table 1.

Table 1. – WHO categorisation of AMs with respect to their importance for human health

Category	Description
Criterion 1	An antimicrobial agent which is the sole, or one of limited available therapy, to treat serious human disease.
Criterion 2	Antimicrobial agent is used to treat diseases caused by either: (1) organisms that may be transmitted to humans from non-human sources or, (2) human diseases caused by organisms that may acquire resistance genes from nonhuman sources.
Critically important	Those antimicrobials which meet both Criterion 1 and Criterion 2 are termed: critically important for human medicine.
Highly important	Those antimicrobials which meet either Criterion 1 or Criterion 2 are termed: highly important for human medicine.
Important	Those antimicrobials which meet neither Criterion 1 nor Criterion 2 are termed: important for human medicine.

Current farm animal veterinary examples of critically important AMs are highlighted in Table 2. Within this group, there is particular concern over the use of third and fourth generation cephalosporins, fluoroquinolones and macrolides in food producing animals.

Table 2. Antimicrobial classes deemed critically important for human medicine which are currently licensed for use in food producing animals in the UK. Classes where there is particular concern over current use in food producing animals are marked with an asterisk.

Class		Farm animal veterinary examples
Aminoglycosides		Dihydrostreptomycin, Framycetin, Kanamycin, Neomycin, Streptomycin
Cephalosporins*	Third generation	Ceftiofur, Cefoperazone
	Fourth generation	Cefquinome
Fluoroquinolones*		Danofloxacin, Enrofloxacin, Marbofloxacin
Macrolides*		Gamithromycin, Tildipirosin, Tilimicosin, Tulathromycin, Tylosin
Penicillins		Ampicillin, Amoxycillin, Penicillin G, Penethamate hydroiodide

However, co-selection for AMR means that simply reducing the use of these classes alone is insufficient to tackle the challenge of AMR, although it should slow resistance development to these classes. For example,

use of tetracyclines may select for cephalosporin resistance in certain cases (Kanwar and others, 2014). Thus, as total antimicrobial use on farm is the biggest driver of AMR, it is this that must be tackled.

Even so, when selecting therapy on farm, first-line AMs, which may be defined as the narrowest spectrum products appropriate to the likely causal organisms in each, must always be selected in the first instance. This excludes critically important AMs.

Developing and implementing a practice policy for responsible medicines use

Governing principles

In order to effectively develop and fully implement a practice policy for responsible medicines use, the following principles are important

- **SMART (Specific, Measurable, Achievable, Relevant and Time-bound) objectives** – Local knowledge of the existing practice approach, established patterns of use and attitudes of VS and farmers is invaluable when it comes to developing a practice-specific AM policy. It is important to consider what general principles of good practise would look like when applied to the specific practice context. This will enable any plan for change to be both prioritised and realistic, with a clear expectations of the timeframe in which objectives may be achieved. Establishment of these approaches will inevitably depend on and be relevant to the starting point, in terms of pre-existing attitudes and current prescribing practices. For example, one objective might be to include discussions on medicines use a part of HHM reviews, another might be to target reducing the use of fluoroquinolones. A third could include running a series of farmer meetings or producing some newsletter articles to raise awareness amongst the client base. Outcomes should be measurable (e.g. achieving a 20% reduction in the total mass of 3rd and 4th generation cephalosporins used), so progress can be demonstrated, recognised, rewarded and encouraged. Start small and build momentum. The Anglo-Irish politician and philosopher Edmund Burke (1729-1797) once said *“Nobody made a greater mistake than he who did nothing because he could only do a little!”* The objectives will inevitably change with progress, but clearly defining smaller objectives allows progress to be measured and success to be recognised and praised.
- **Strong leadership and cultural change** – As with other aspects of clinical governance, strong and enthusiastic leadership can help to achieve change. In some practices this will involve significant cultural change. Directly challenging the established status quo and confronting the opinions and practices of influential, potentially senior members of staff may be required. A wider adoption of EBVM goes hand-in-hand with this approach, because establishing cultural norms for practice becomes more about the science than about personalities and opinions based on anecdotes and seniority, unsubstantiated by clear evidence.
- **Practice-wide involvement** – It is essential that all members of the practice team take ownership of responsible medicines use within the practice: they must understand and commit to both developing and supporting the implementation of any practice-wide policy, particularly with respect to critically important AMs(Figure 3). This cannot be a solo effort if it is to be sustainable. It is especially important for support and administrative staff – particularly those who are client facing or with responsibility for pharmacy management or dispensing – to take a central role. Practical solutions might involve a traffic light system to colour code pharmacy shelves or established prescribing lists

for each farm. If the whole practice team is involved in presenting a coherent and consistent message to the client base and the VSs routinely model the same diligent approach to responsible prescribing, then the impact will be greater. Training of staff at all levels is critical, in order to equip the whole team with the skills and resources necessary for change.

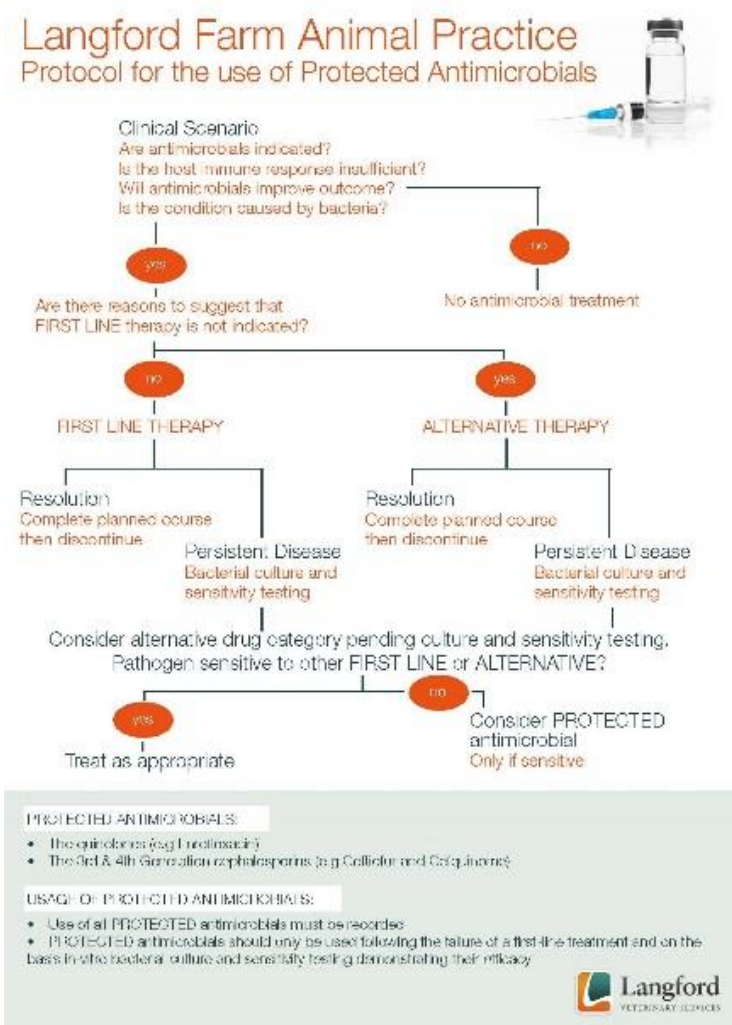


Figure 3. Langford Farm Animal Practice: Protocol for the use of critically important antimicrobials.

(The term protected antimicrobials here refers to third and fourth generation cephalosporins, fluoroquinolones and the longer acting macrolides).

- **Participatory and collaborative** – The team at Langford Farm Animal Practice (LFAP), a clinical teaching practice of the University of Bristol, School of Veterinary Sciences, found that one of the key factors for success in achieving behavioural change towards more responsible use amongst farmers and VSs was adopting a collaborative approach. Farmers were drawn in as partners in the process, and practice policy and behavioural change moved forwards together. A concerted programme of client education through intentional farmers' meetings and targeted newsletter articles was important, but it was the intentional one-to-one, on-farm conversations as part of HHM that helped to make change sustainable. The challenge of responsible medicines use needs to be one that farmers and VSs tackle together, though the leadership from this should come from veterinary practices.

- **EBVM-driven** – Farm animal VS must have the skills and knowledge required for rational, responsible prescribing, be able to critically review medicines use on farm within the context of HHM and be skilled in motivating very necessary change in this area. In the absence of widely available, rapid, patient-side diagnostics, in the short-term, the majority of prescribing decisions will still be made on an empirical basis. Therapeutic best-practice, as far as can be established from the available evidence base, should be the starting point. Excellent online training resources to support VS in the application of EBVM to clinical practice are available through EBVM Learning (www.ebvmlearning.org), funded by RCVS Knowledge. Existing good-practice guidelines should be adopted, for example the BVA 7-Point Plan (Figure 4) and the Responsible Use of Medicines in Agriculture (RUMA) Alliance guidelines (RUMA, 2015). It is the intention of the Veterinary Medicines Directorate (VMD) that the UK Veterinary Antibiotic Resistance and Sales Surveillance (UK-VARSS) report should influence and inform prescribing habits and herd health management decisions on farm (VMD, 2013)



Figure 4. BVA 7-Point Plan: Responsible use of antimicrobials in veterinary practice

- **Client education** – Given that in farm animal practice the majority of treatments are administered by animal keepers, rather than VSs, it is critical that farm clients are actively involved in the process of change. The VS and farmers must embark on a journey of change together where the need to challenge current practices can be established first, before a shared way forwards is agreed. Client education is key, taking the form of farmers’ meetings or newsletter articles. It is important to start where your clients are. Participatory approaches often work best with farmers having an opportunity to learn from one another, with or without farm level benchmarking as a starting point for discussion, however, the importance of the individual, one to one, VS to farmer dialogue should not be underestimated. Using the theory of planned behaviour, a recent UK study established that the strongest driver to reduce AM use was the perception that their social networks and advisers would approve of this (Jones and others, 2015). Veterinary Surgeons have the potential to be highly influential in affecting behavioural change and should be equipped to do this, through appropriate communication skills training (e.g. motivational interviewing). The critical step is that the approach needs to be participatory and the farmers need to ‘buy in’ to the process. Simply telling clients what you think they should do, will not bring about lasting behavioural change!

- **Sustainability** – Developing a culture of practice that lasts is essential; to be sustainable, change must extend beyond the influence of a small number of key individuals who may have been important in the conception and introduction of new approaches, but cannot carry them forward in isolation or indefinitely. Establishing agreed written protocols can help, but this needs to be more than a paper exercise. Habituating staff to an ongoing process of training, discussion and re-training within this area is key. Internal CPD training for inexperienced staff and, if appropriate, re-training of experienced members of the team will help to ensure that training can be sustained. Practice policies on antimicrobial use should form part of the induction process of any new member of staff, regardless of their role within the practice. Responsible medicine use must become the cultural norm within the practice and be embedded in, and underpin, every aspect of clinical practice.
- **Clinical governance and auditing medicines use** – In order for antimicrobial use to be considered truly responsible, it must be measured, monitored and reviewed by farm animal Vets, as should all other aspects of HHM. Systematic farm- and practice-level medicines auditing is a useful way in which this can be achieved. Audits such as these identify key opportunities for improvements, allow benchmarking of progress, and have played an important role in changing patterns of antimicrobial use within the LFAP (Tisdall and others, 2015).

Case study: Langford Farm Animal Practice

The LFAP has a long history and developed culture of proactively engaging with farm clients to encourage responsible AM use. Reducing total AM use while driving more responsible use on farms – optimising AM use – is likely to have the biggest impact in slowing AMR development (Department of Health, 2013).

Approach

A collaborative approach, working alongside farmers to improve HHM and informed by systematic farm-level medicines auditing coupled with farmer training and intentional changes in prescribing policy has proved highly successful in achieving this change (Figure 5). Farmers' meetings and regular newsletter articles were used to raise awareness, provide training on compliance and responsible antimicrobial use and to encourage engagement by farmers.

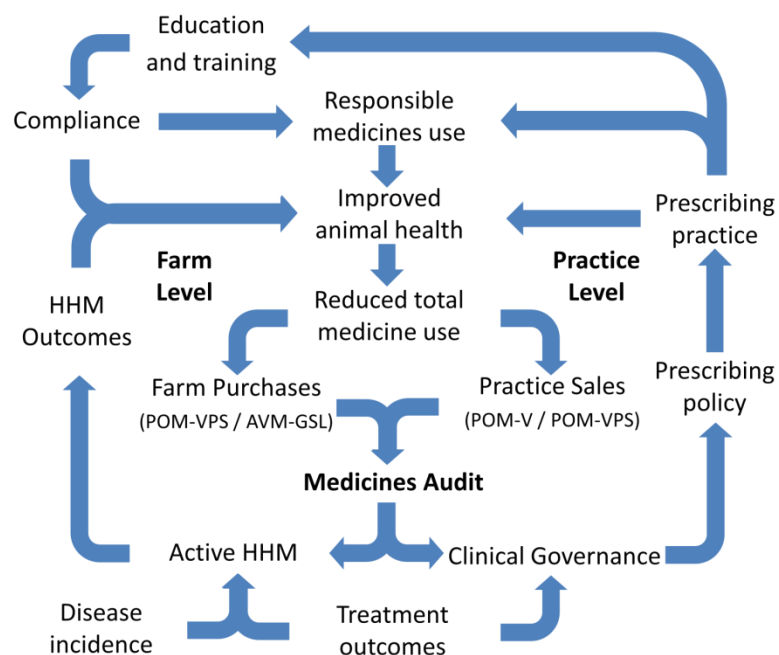


Figure 5. Integration of medicines audits with HHM and clinical governance

Consideration of both animal health and economic implications of current medicines use - including the balance between preventive interventions (e.g. HHM, vaccination and non-antibiotic dry cow therapy) and reactive treatments (e.g. systemic antibiotics, lactating cow therapy and non-steroidal anti-inflammatory drugs) - allowed targeted recommendations to both reduce disease and improve profitability. Areas of good practice and responsible medicines use were identified, emphasised and encouraged, and poor compliance highlighted.

Table 3. illustrates the major practice level changes in AM prescribing policy.

Table 3. Major practice level changes in AM prescribing policy

Area of use	Changes in prescribing policy
Intra-mammary use	Fourth-generation cephalosporins phased out in favour of penicillin and aminoglycoside combinations
Systemic use	Fluoroquinolone use halted. Third- / fourth- generation cephalosporins were replaced with first-generation cephalosporins or aminopenicillins.
Calf pneumonia	Longer-acting macrolides were replaced with oxytetracycline or florfenicol and a greater emphasis placed on non-antimicrobial therapies (e.g. NSAIDs).

An annual retrospective analysis of medicines use data at practice level from 2010 onwards was carried out to assess the impact of this approach. Multiple measures were used to benchmark medicines use. In particular, animal daily dose (mg/kg/day) and number of doses or courses per animal year at risk have been used at farm level, when herd size and profile could be accurately established. Economic measures (e.g.

pence per litre on medicines spend) were also included. At practice level, due to the broad range of species catered for, total milligrams used per year was found to be an appropriate metric to monitor total use.

Results

Between 2010 and 2015, a 100% reduction in intramammary use and a 91% reduction in the systemic use of certain critically important antimicrobials (CIAs) has been achieved, namely third- and fourth-generation cephalosporins, fluoroquinolones and long-acting macrolides (Figure 6). Total antimicrobial use was reduced by 7% between 2014 and 2015, having remained relatively static for the previous five years against a 10% increase in dairy cattle numbers (Figure 7). No fluoroquinolones have been used since 2009.

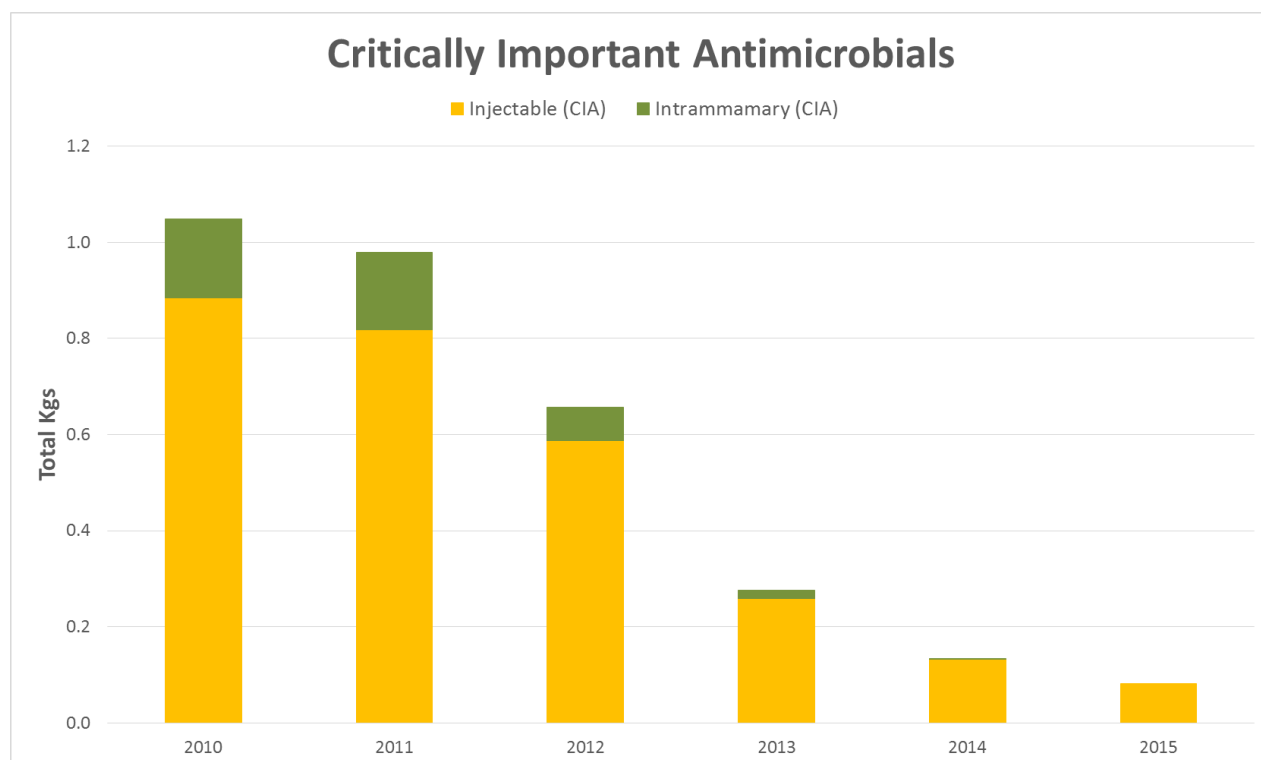


Figure 6 – Use of antimicrobials critically important for human health

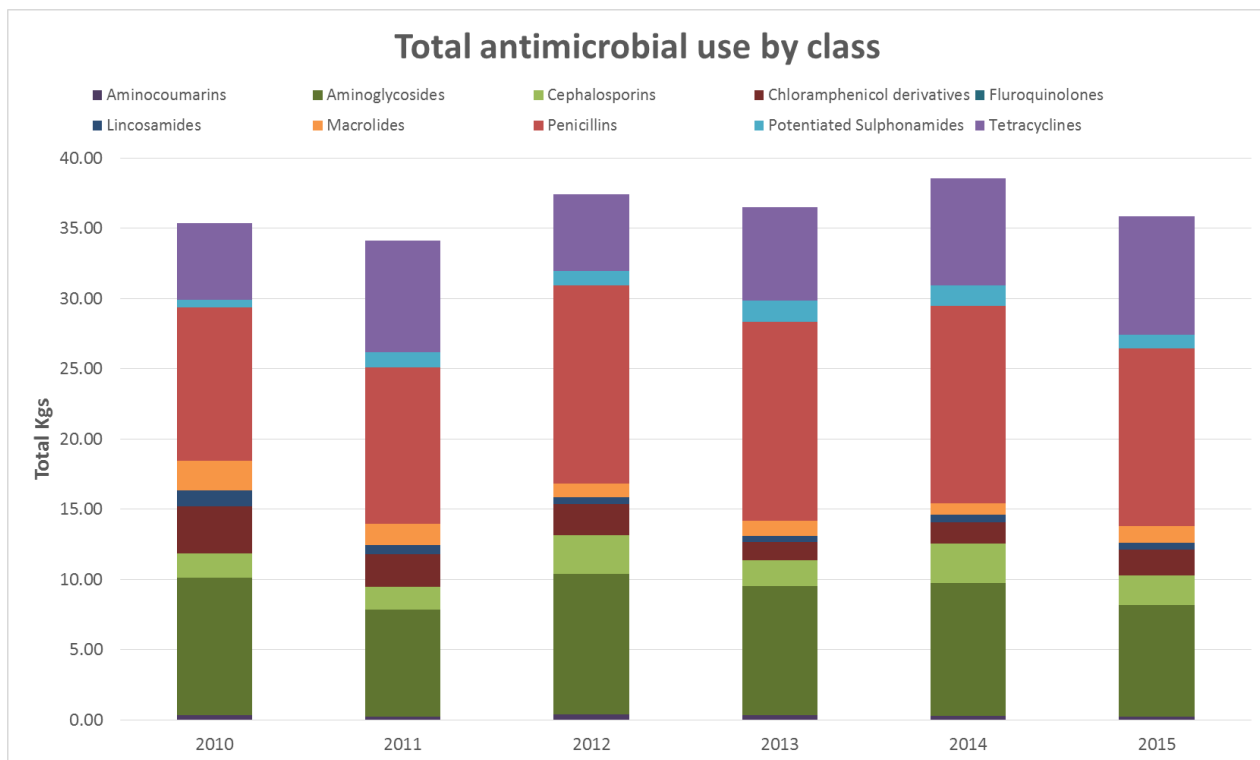


Figure 7 – Total antimicrobial use

Although total antimicrobial use at practice level in the LFAP has remained relatively constant. In real terms, this actually represents a reduction in the number of courses of antimicrobials prescribed per animal, given factors such as 1) the 10% increase in dairy cattle numbers, 2) the training emphasis placed on accurate dosing and course completion, and 3) the relatively higher dose rates of alternative products (e.g. the dose rate of amoxicillin is 7 mg/kg compared to 1 mg/kg for ceftiofur).

There was no evidence of declining herd health or cure rates (whether real or farmer-perceived) with a move away from the use of CIAs. Improved farm management and preventive strategies have continued to lead to reduced levels of disease. Clinical mastitis is one such example, demonstrating a 32% reduction in the use of lactating cow therapy (Figure 7). Dairy farm-level disease incidence data also supports this conclusion (data currently under analysis).

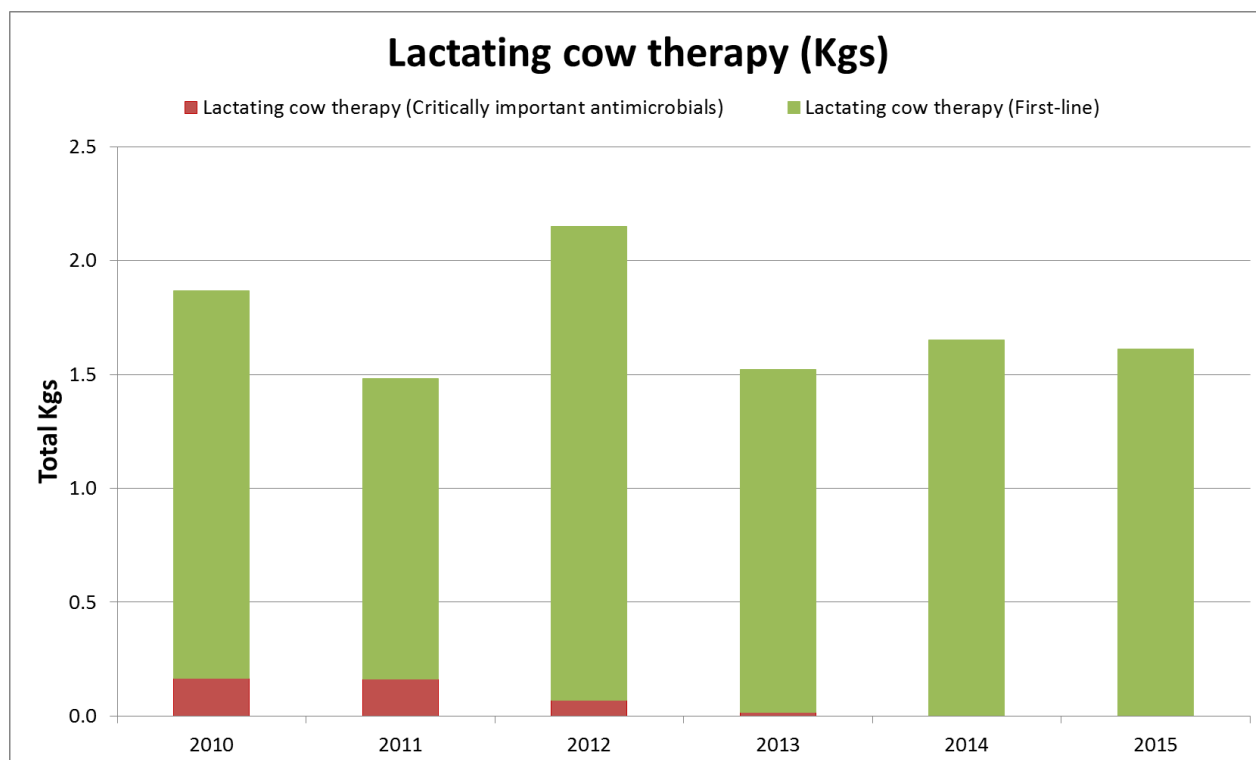


Figure 7. Use of lactating cow therapy for the treatment of clinical mastitis

Concern over farmer willingness to participate in change, although widely discussed, was proved to be unfounded. It is likely that the collaborative approach employed by LFAP practitioners and clients contributed to success, building upon the existing, well-developed relationship of trust between farmers and practice VSs. Farm clients have been consistently positive about tackling the issues of responsible medicines use and AMR in partnership with the practice. This is consistent with the findings of Jones and others (2015).

Challenges to systematic medicines auditing

Establishing correct benchmarks

Careful consideration should be given when considering appropriate benchmarking measures.

The first challenge is defining the most appropriate measures for medicines use at farm level, bearing in mind that context and the user (e.g. VS, farmer or central authority) will influence what are the most appropriate measures. Defining the population at risk is challenging. For this reason, total kgs of antimicrobials may be a more appropriate measures at practice level, particularly when a diverse range of species and types of animals are cared for.

Informal feedback suggests farmers have found measures which express antimicrobial use in terms of doses, courses or economics most useful.

Making the correct assumptions

When using information about practice medicines sales as a proxy for on-farm medicine use, assumptions about data quality, standard treatment protocols and background population are unavoidable. Cross-checking these assumptions against on-farm practise is key, but can also be a useful and informative part of the HHM review and arguably something that should be happening anyway to ensure responsible use. There will be some inaccuracies in medicines sales data extracted from practice recording systems; the completeness and accessibility of these, however, are likely to exceed that of on-farm treatment records, making them a valuable data resource.

Conclusions

Changes to prescribing practices as described here may have reduced the selection pressure for AMR. On dairy farms, recent use of third- and fourth-generation cephalosporins is strongly associated with an increased likelihood of the presence of extended-spectrum beta-lactamase *E. coli* (specifically CTX-M), while use of first and second generation cephalosporins is not similarly associated (Snow and others, 2012).

For veterinarians interested in responding to the threat of AMR, this work shows it is possible to achieve marked reductions in the use of critically important antimicrobials in food-producing animals alongside reductions in total use, whilst keeping farmers on board and continuing to improve animal health and welfare, and without the need for legislation. The continued use of CIAs as first line treatments cannot be justified and should be phased out as a matter of priority. The need for change is clear and our experience is that farmers are keen to play their part. We do not need to wait for legislation to force change upon the livestock sector, these very necessary changes should be led by the veterinary profession now in collaboration with livestock producers.

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Conflicts of interest

None.

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